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Model Predictions and Measured Skin Damage Thresholds for 1.54 μm Laser Pulses in Porcine Skin

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ABSTRACT

A new source-term thermal model was used to determine the skin temperature rise using porcine skin parameters for various wavelengths, pulse durations, and laser spot sizes and is compared to the Takata thermal model. Expanding on this preliminary source-term model using a Gaussian profile to describe the spatial extent of laser pulse interaction in skin, we report on the coupling of temporal consideration to the model. Computer simulation of the new source-term model and the Takata thermal model are presented to highlight the theoretical extent of thermal damage. Laser exposures of 1.54 μm, 0.60 ms in duration and using spot sizes of 0.7 mm and 1.0 mm were applied to the porcine skin. The damage thresholds were determined at 1 hour and 24 hours post-exposures using probit analysis. The ED_{50} for these skin exposures at 24 hours post-exposure were 20 J/cm^{2}and 8.1 J/cm^{2}respectively. These damage thresholds are compared with our model predictions and another thermal model with the damage integral predicting damage levels. They are also compared with previously published skin thresholds and with the ANSI Standard's MPE for 1540 nm lasers at 0.60 ms.

Key Words: laser safety, laser skin model, skin injury Er:Glass, temperature rise

Introduction

One of the most common lasers wavelengths in the far infrared region is 1.54 micrometers (μm) that is generated using a glass rod doped with Erbium ions (Er:Glass laser rods). These rods can produce energies exceeding tens of joules per pulse for millisecond pulse durations. The American National Standards Institute[1] (ANSI), Z136, divides the electromagnetic spectrum into bands of wavelength regions. Wavelengths from 1.4 μm to 100 μm are considered the far infrared while the near infrared is defined as the region ranging from 0.7 μm to 1.4 μm. Infrared laser technology has matured enough so that they are now being used by the military, industrial and commercial applications in many devices and systems. For example, many navigational and targeting systems used by the Air Force and Navy, as well as the rangefinders used by the Army, utilize this laser wavelength with various pulse energies, pulse durations, beam profiles and spot sizes. Several commercial application have been developed, including soldering blood vessels and tumor removal from human skin with the Er:Glass laser.[2]

From its beginning, the 1.54 μm wavelength was referred to as "eye safe" and has maintained that misnomer in the commercial arena. "Eye safe" refers only to the retina and not the cornea or lens of the human eye in this context. The current ANSI laser standard, Z136.1-2000, defines a maximum permissible exposure[1] (MPE) to both the eye and the skin for this wavelength that

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depends upon the pulse duration. For example, pulse durations ranging from 10^{-9} seconds (1 ns) to 10 seconds for 1.54 μm is set at 1 Joule per square centimeter (J/cm^2) for small-source exposures. The MPE in the ANSI Z136.1-2000 is set to insure that no damage to the cornea or skin occurs for exposures at or below the MPE. Therefore, above the ANSI Z136.1-2000 MPE for 1.54 μm a skin and cornea hazard can exist, negating the term "eye safe". For a thorough understanding of laser hazard evaluation methods, see Marshall et al.[3]

Mathematical models allow for the comparison of data between researchers and can be incorporated into the ANSI laser safety standards to make predictions of the MPE for a much broader range of wavelengths, pulse durations, exposure conditions and subject materials. One mathematical model that we are using was developed at Brooks AFB, TX in the early 1970s (the Takata thermal model) and is being run on a Linux machine from Fortran code. It consists of three separate parts: one model for the retina, one for the cornea and another model for skin. All three use the same heat-conduction equation and the rate-processes to obtain damage thresholds. These models were originally developed for the visible wavelength bands and they were validated using non-human primate eyes and porcine skins.[8,9] They have since been revised and extended to include infrared wavelengths and temperature rises. Damage thresholds are calculated for various wavelength, pulse durations, spot sizes and parameters from this model. One data file contains parameters for the cornea, one for the retina and a separate file for the skin. Calculations can be performed on all three tissue model types for wavelengths out to 10.6 microns.

The new source-term thermal model was developed to help understand the inability of the Takata thermal model to determine reasonable theoretical damage endpoints for laser exposures whose spot diameters were less than 1.0 mm. In addition we have computed the temporal term in the source-term thermal model assuming a Gaussian fall off when compared to the pulse for a dispersive media. For example, if the pulse duration is 0.60 ms then within the first 0.60 ms after the initial exposure the temperature rise will fall to the $1/e^2$ value of the maximum temperature achieved. Further, we can analytically compute the mean value temperature rise using the integral mean value theorem for the spatial extent of the source-term temperature model.

To date, very few damage threshold measurements have been reported in the literature for 1.54 μm and the reported values vary to such a wide extent that additional measurements are required to support ANSI Z136.1-2000's revision. Laser induced damage to porcine skin has been reported for the 1.54 μm wavelength for large spot sizes by Lukashev, et al.[4,5] They report the damage threshold for a spot size of 5.5 mm in diameter for two different pulse durations, 3 ms and 100 ns. For small spot sizes, Rico, et al[6,7] reported similar measurements but with different thresholds. In this work two new spot sizes with ED_{50} measurement for 1.54 μm are reported with a comparison to two mathematical thermal models.[8,9] So far, reported values in the literature were taken at different spot sizes and pulse durations leaving a series of experiments to be conducted that will extend the database for ANSI Z136.1 consideration with consistent input parameters. Further, there is a great need for mathematical modeling that can make accurate predictions of the MPE's based upon threshold endpoints (ED_{50}'s) and provide for a reduced number of experiments. It is anticipated that such a model would provide reliable predictions for any type of laser for different pulse durations, wavelengths and spot sizes.

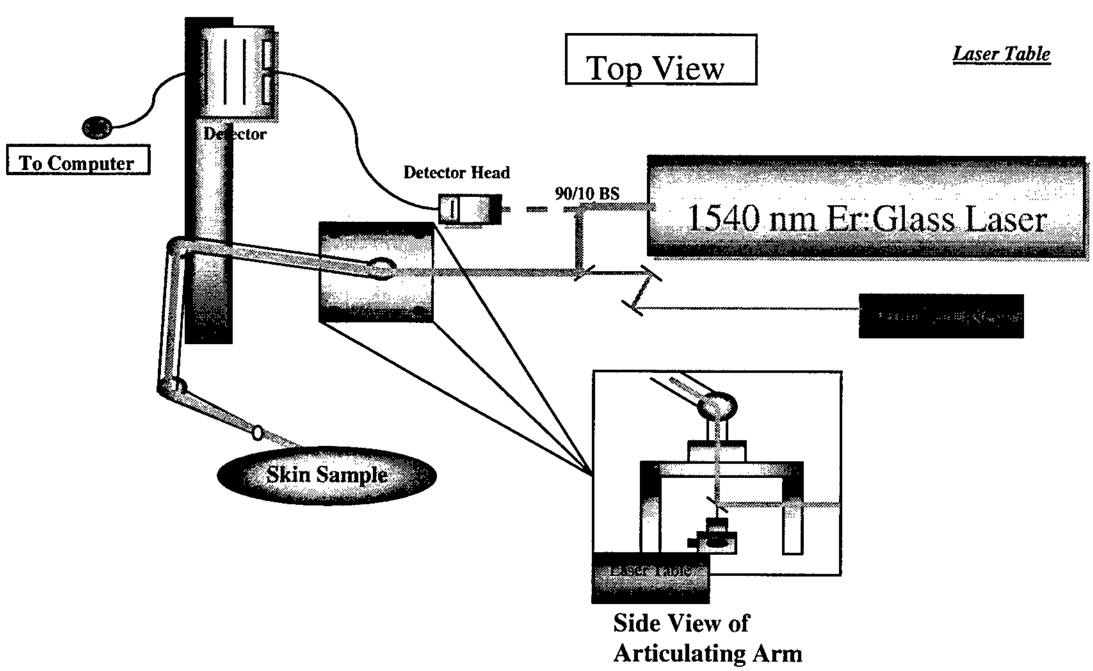
This study uses the Yucatan mini-pig (*Sus scrofa domestica*) as the model to determine the estimated dose for 50% probability of laser-induced damage (ED_{50}) for laser injury to skin at 1540 nm wavelength for a single 0.60 ms pulse duration exposure because the Yucatan mini-pig model has been found to have higher anatomical similarity to human skin than the commonly used Yorkshire mini-pig model[5]. Yucatan mini-pig skin is melanated and, on the flank, is of

similar thickness to that on the human arm, which has high probability of accidental exposure. By using this model, the properties of human skin can be more closely approximated to gain a better understanding of the human laser-tissue interaction for the wavelength of interest. The data on porcine skin damage obtained from this study will contribute to the further understanding of laser injury mechanisms and will add to the existing data on laser-skin effects, on which safety standards are based and which affect employment of these laser systems.

Materials and Methods

Laser exposures were accomplished with a laser system (Laser Sight Technologies Inc. Orlando, FL) using an Er:Glass rod, delivering 1540-nm light at 0.6-ms exposure time, and at various pulse energies. The laser produced a Gaussian beam profile, and two experimental spot sizes (0.7 mm and 1.0 mm) were used in this study. Spot sizes were measured using an Electro Physics IR camera with a Spiricon LBA 500 Laser Beam analyzer and beam grabber card. The pulse duration was measured by an ET-3000 InGaAs Electro-Optics Technology, Inc. (Traverse City, MI) photodiode connected to a Tektronix TDS 220 oscilloscope. Energy measurements are made with a Molectron JD1000 energy meter and J25 and J50 energy probes, which were placed after a 90/10 beam splitter to collect 10% of the beam energy, and thus determine the actual energy delivered to the skin. An articulating arm laser beam delivery system from Laser Mechanisms, Inc, was used to deliver the beam without having to move the subject. A metal "aiming ring" was attached to the end of the articulating arm, which maintained a constant distance between the arm's aperture and the subject. This allowed for precise positioning and distance control necessary to deliver exposures of known spot-size, more accurate beam delivery and a higher number of exposures per subject, resulting in a reduction of the total number of subjects required. The laser system setup is depicted in Figure 1.

Figure 1. Block diagram of experimental setup for delivering 1540 nm pulses to skin



Five female Yucatan mini-pigs (Lonestar Laboratory Swine, Seguin, TX), weighing between 15 and 20 kg, were involved in this study. Four separate flanks were used at each spot size. Animals were between 3 and 8 months of age. The study fell under the animal use protocol titled "Evaluation of Laser induced Corneal Lesions in the Dutch Belted Rabbit and Skin Lesions in the Yucatan Mini-Pig," which was approved by the Brooks City-Base, TX Institutional Animal Care and Use Committee (IACUC). None of the animals were euthanized after exposure or biopsy, since they were part of an animal-sharing program. Pigs were fed standard, commercially available diets, and had unlimited access to water. However, solid food was withheld for 12 hours prior to laser exposure and biopsy collection. The animals involved in this study were procured, maintained, and used in accordance with the Federal Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources -- National Research Council. Brooks City-Base, TX has been fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) since 1967.

The pigs were sedated by single syringe injection of Tiletamine/Zolazepam (4-6 mg/kg) intramuscular (IM) and Xylazine (2.2 mg/kg) IM, and maintained on inhalation isoflurane anesthesia during all procedures. After sedation, hair on the flank was clipped using hand clippers, and the cleansed skin was inspected by each of three evaluators to check for redness, irritation or other confounding marks. Physiological parameters were monitored throughout all procedures. Buprenorphine (0.05-0.1 mg/kg) was administered intramuscularly for analgesia after biopsies were complete. The animals were returned to their runs upon recovery to sternal recumbency from anesthesia.

For each subject, the flank to be exposed was marked with two 6 cm x 6 cm grids with a permanent-ink Sharpie marker (see Figure 2A), making a total of 72 grid squares per flank. As previously mentioned, the distance between the articulating arm aperture and the skin was kept constant by the use of a metal device attached to the end of the arm. The animal, positioned on a table, did not have to be moved during procedures. Energy was delivered randomly to one grid at systematically varied intensities, and this process was then repeated on the second grid.

Yucatan mini-pigs were used as the skin model for this study.[11] Subjects were received from an attendant veterinary technician via stretcher, sedated, with indwelling intravenous catheter placed in an ear vein, and intubated prior to arrival at the laboratory. Upon arrival, the subjects were taken to the laboratory where flanks for exposure were selected, clipped with electric clippers, cleansed with chlorhexadine solution and allowed to air dry. All subjects were kept warm during the entirety of the procedures. Post exposure: Three 5 mm punch biopsies were obtained from each subject immediately after the 1-hour post exposure reading and again after the 24-hour reading: one of the three biopsy sites on each animal was chosen as a control (taken from a location superior to any exposure sites). All biopsy sites were closed with non-absorbable 2-0 sutures and topically medicated with Trio-mycin ointment for infection prophylaxis.

Probit[10] analysis was the statistical method used to determine the estimated dose for 50% probability of laser-induced damage, ED_{50}, for the in-vivo skin model. Reading of injured sites were performed acutely (10 minutes post exposure), at one-hour and at 24-hours post exposure. All data points were entered into the probit statistical analysis package and the ED_{50}'s were calculated along with their fiducial limits at the 95% confidence level, slopes and probabilities. Two out of three readers were required to determine if a lesion was a present or not.

Results

Threshold measurements for two spot sizes have been accomplished and enough exposure sites and data points were taken to provide the ED_{50} using probit analysis along with the fiducial limits at the 95% confidence level. For both the 1-hour and 24-hour post-exposure readings the ED_{50}s are listed in Table 1 along with their fiducial limits and slopes of the probit curves (Slope = $\delta p / \delta d$ where δp = delta probability and δd = delta dose).

Table 1. MVL-ED50 data at 1 hour and 24 hours post-exposure for 1540 nm laser pulses.

Experimental Setup Number of Subjects & Shots	MVL-ED_{50} (J/cm^2) 1 Hour Reading	MVL-ED_{50} (J/cm^2) 24 Hour Reading	Probit Curve Slope = $\delta p / \delta d$
0.7 mm diameter laser beam 4 pigs, 4 flanks, 263 exposures	26 (30 – 23)	20 (21 – 18)	5.7
1.0 mm diameter laser beam 3 pigs, 3 flanks, 216 exposures	11 (11 – 9.5)	8.1 (8.7 – 7.5)	15

Most of the immediate lesion showed up as a blotched red coloring near the center of the square where the laser beam penetrated the skin. These red spots appeared almost immediately and most disappeared before the 1-hour reading. Exposures sites could be observed visually after 1 hour except they were no longer red splotches but very small discolorations in the skin. At the 24-hour post exposure reading, more lesions could be clearly observed than were visible at 10 min or 1 hour post exposure. The ED_{50} was reduced between the 1 and 24-hour endpoints for both spot sizes as shown in Table 1.

Additional probit runs were made for the 0.7-mm diameter spot size when it was noticed that the probability of Chi-sq for the 24 hr reading was a very low value of 0.0057 while the Pearson's Chi-sq was a value of 208. For the 279 exposures read at 24 hours, the fluences ranges from 4.9 to 51 J/cm^2 and it was determined that several zeros were observed for the high-energy exposures. Another set of data was run with all exposures of 42 J/cm^2 and above eliminated which now gave the same threshold but with the Chi-sq increased to 0.48. This same set of data was decreased to a maximum of 33 J/cm^2 for the top exposure and the Chi-sq was again increased to 0.89 without changing the threshold of 20 J/cm^2. Pearson's Chi-sq was decreased from 208 to 108 for this run. Fiducial limits for all 3 conditions were all within $\pm$ 10% of their ED_{50} values. These changes when applied to the 1-hour reading did not significantly affect any parameters. Since the Chi-sq for the 1-mm diameter spot size was 1.00 at the 1-hour and 24-hour reading, nothing could be changed to increase these values.

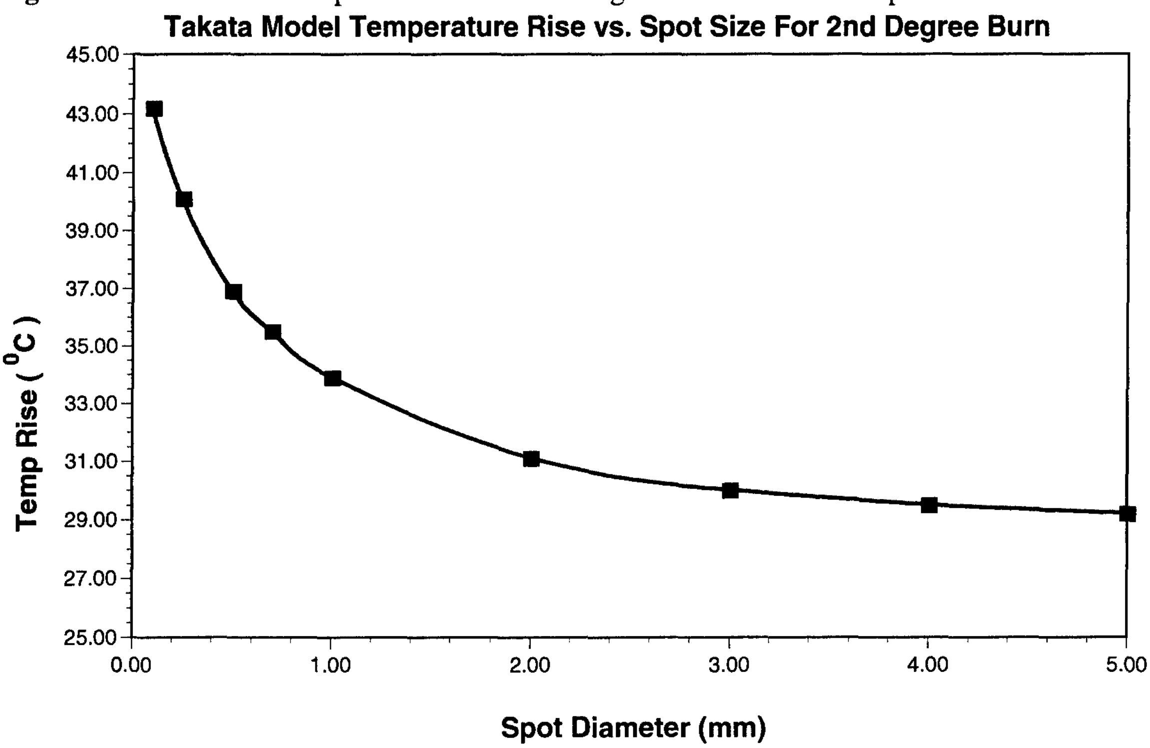
Modeling Results

Calculations from the Takata thermal model for skin are listed in Table 2 for minimum 2nd degree burns calculated for various pulse energies and spot sizes. Laser exposure diameters were varied from 0.1 mm to 5 mm diameters and the laser pulse powers were varied to determine the minimum power required to provide a minimum 2nd degree burn. Minimum temperature rises are plotted as a function of spot diameter in Figure 2 for those values listed in Table 2. Fluences (J/cm2)

Table 2. Takata 2^{nd} Degree Burn Model Outputs for 8 spot sizes using latest parameters for Skin

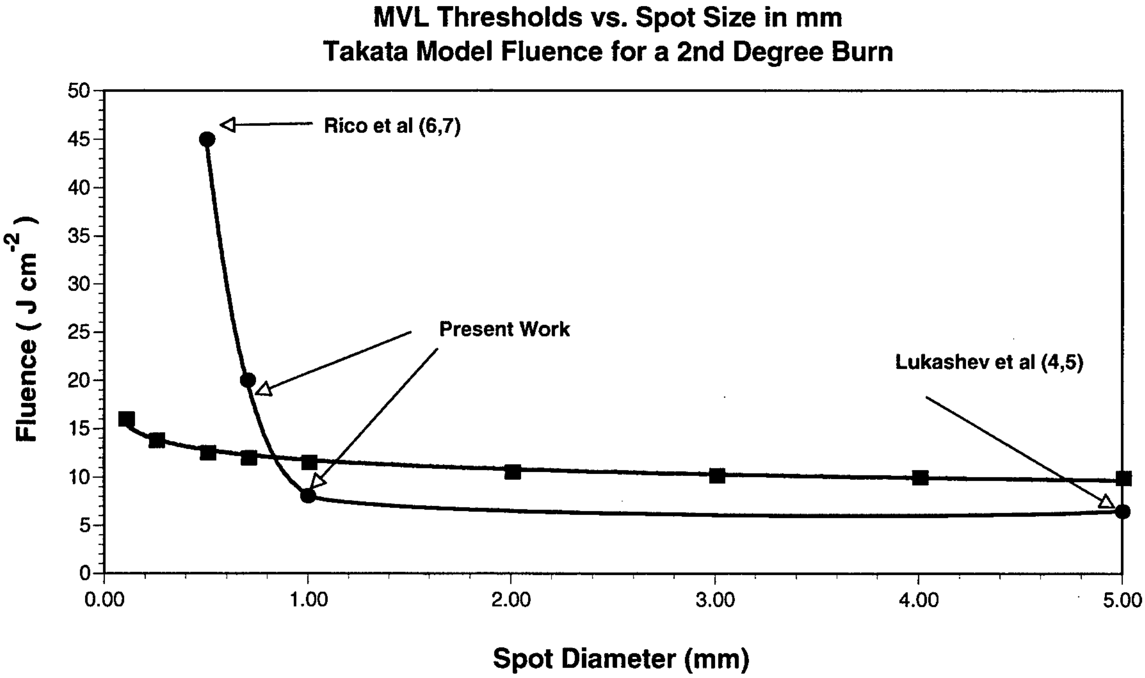
Spot diameter (mm)	Pulse Energy (J)	Power (W)	T (°C)	Fluence (J/cm^2)
0.10	0.00126	2.1	43.2	16.04
0.25	0.00678	11.3	40.1	13.81
0.50	0.0246	41.0	36.9	12.53
0.70	0.0462	77.0	35.5	12.00
1.00	0.0906	151	33.9	11.54
2.00	0.3324	554	31.1	10.58
3.00	0.72	1200	30.0	10.19
4.00	1.26	2100	29.5	10.03
5.00	1.95	3250	29.2	9.93

Figure 2. Takata Model temperature rises for 2^{nd} degree burns for various spot diameters



required to produce these temperature rises are listed in Table 2 and are plotted in Figure 3 together with the MVL-ED_{50} data at 24 hours listed in Table 1 and two other data points from the literature. In this Figure 3 it can be seen how closely the Takata skin model computes the thresholds as measured in the laboratory for fluence values with an exposure spot diameter equal to or greater than 1.0 mm.

Figure 3. Thresholds for 2nd degree burns and MVL-ED_{50} thresholds versus spot sizes

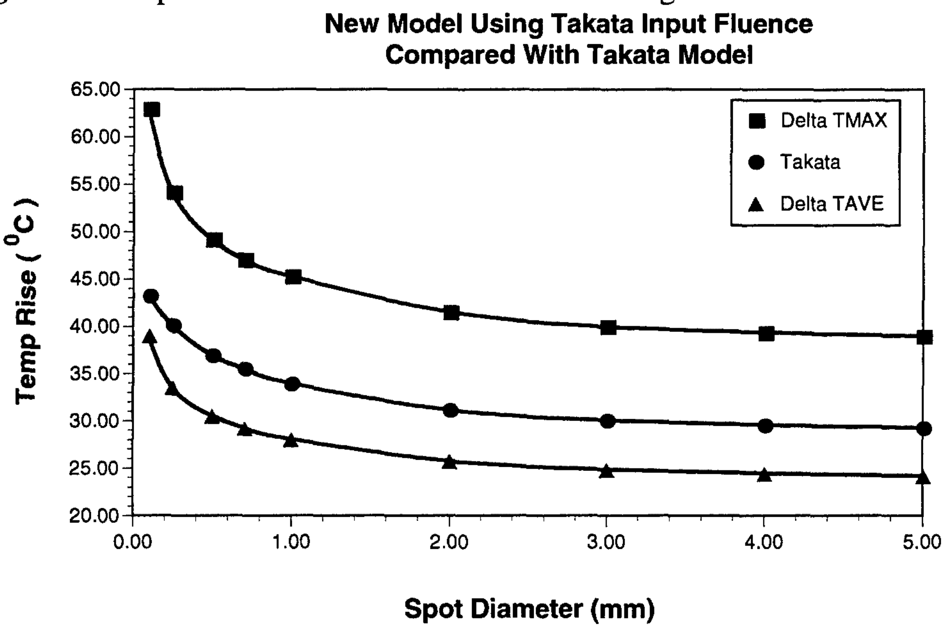


In Table 3 we show the comparison of the new source-term thermal model to that of the Takata skin model values obtained from Table 2. We note that at the smallest input spot diameter of 0.10 mm, the difference between the Takata temperature and ΔTMAX is 19.7 °C versus the largest spot diameter at 5.0 mm of 9.7 °C. When comparing the Takata values with the ΔTAVE, at the smallest spot diameter input one notes a difference of 4.2 °C and at the largest spot diameter a difference of 5.1 °C. Figure 4 plots the values in Table 3 for comparison between the two models. One striking feature is noted in Figure 4, the appearance of the sharp up turn in the ΔTMAX and ΔTAVE values below 1.0 mm when compared to the Takata temperature rise below the same point.

Table 3. New Thermal Model Outputs Compared to the Takata Skin Model for 2nd Degree Burn

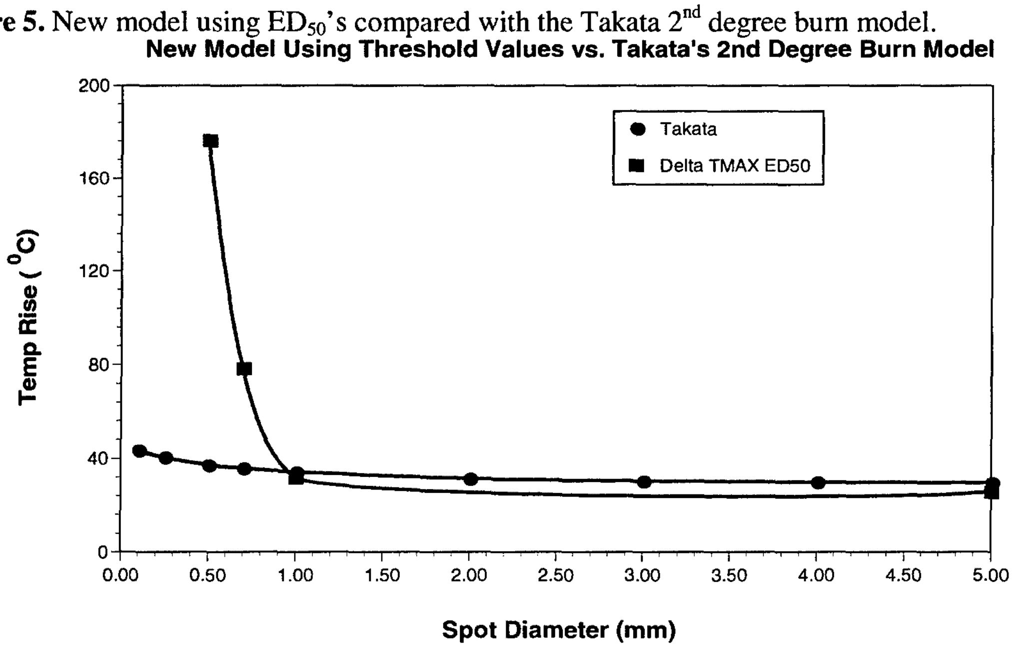
Spot Diameter (mm)	Fluence (J/cm^2)	Takata Temp (°C)	ΔTMAX (°C)	ΔTAVE (°C)
0.10	16.04	43.2	62.9	39.0
0.25	13.81	40.1	54.1	33.5
0.50	12.53	36.9	49.1	30.5
0.70	12.00	35.5	47.0	29.2
1.00	11.54	33.9	45.2	28.0
2.00	10.58	31.1	41.5	25.7
3.00	10.19	30.0	39.9	24.8
4.00	10.03	29.5	39.3	24.4
5.00	9.93	29.2	38.9	24.1

Figure 4. Comparison of New Model to Takata 2nd degree burn model



In Figure 5 we show the comparison of the new source-term thermal model to that of the Takata skin model as a function of temperature rise versus laser spot diameter. Here ΔTMAX is computed for the ED_{50}'s from the literature and the current work and plotted against the Takata skin model temperature rise for 2nd degree burns found in Table 1. We note relatively good agreement with Takata at and above 1.0 mm, but a dramatic departure below 1.0 mm where the Takata skin model does not predict a significant temperature rise for laser spot diameters this small.

Figure 5. New model using ED_{50}'s compared with the Takata 2nd degree burn model.



DISCUSSION & CONCLUSIONS

Both thresholds listed in Table 1 at 24 hours post-exposure are lower than those shown at the 1-hour reading. As with all of our past skin threshold measurements, more lesions are visible after 24 hours than at the 1-hour reading. Two other threshold measurements at 1540 nm to the skin have been reported and these are shown in Figure 3 together with our two thresholds for different spot sizes. For the three data points at 1 mm and below in diameter, we see that the measured thresholds increase inversely at a much greater rate than that predicted by the Takata skin model. For our measured threshold at 0.7 mm in diameter we observed a number of flashes at the skin surface for the higher energy laser pulses and for some, we could smell the burned flesh and for others hear a pop. In analyzing the data we discovered that there were a large number of zeros or non-lesions at these very large laser pulse energies. In fact the Chi-square term in the probit analysis was found to be 0.007, showing this distribution was definitely not normal. When we eliminated all data points above certain pulse energies, we raised the Chi-square term to above 0.6 but did not change the ED50 value.

We hypothesize that pulse energies much too large for this spot diameter were used and the energy input was probably creating plasma at the skin surface instead of propagating into the skin where it could create a lesion. We also hypothesize that plasma generation could have occurred at the lower pulse energies but did not give an observable indication as did the higher-energy pulses. Low-density plasmas could have been created without the laser induced breakdown (LIB) producing a visible indication. Thus some of the pulse energy could have been absorbed before the pulse reached the surface of the skin and this would have required a higher-energy pulse to cause a visible lesion. To date we have found no other reason for such a large deviation between model thresholds and the ED_{50}'s below 1.0 mm spot diameters. We note that the Chi-square distribution calculated for the 1.0 mm spot diameter was 1.00 and flashes of light normally associated with LIB production were not observed at this spot diameter. We again hypothesize that the threshold reported by Rico, et al[6], also had LIB and plasmas generated due to its very high threshold and conclude that more data points between 1 and 5 mm should help to clarify this ambiguity.

Both thermal models predict a temperature rise due to energy deposition within the tissue throughout a volume as defined by the input parameters. In the Takata skin model this prediction of temperature rise is based upon power input where the model computes a time step throughout the energy deposition, laser pulse length, and for as long afterwards as necessary to return the temperature back to pre-exposure levels. In contrast, the new source-term thermal model does not and we are challenged now to solve the three dimensional heat transfer equation for better model comparison. As shown in Figure 4 for both models predict a temperature rise necessary to give an injury while being very dependant upon the radiant exposure input spot size. We note that this spot size dependency is greater for spot sizes less than 1.0 mm in diameter as seen in Figure 5. Above a 1.0 mm spot diameter the Takata thermal skin model temperature rises has been correlated with damage levels as a validation of the that model, while below 1.0 mm no correlation is yet possible.

Critical is the interdependence with any rate-process model, therefore dependence on the time-temperature history and not on temperature rise alone must be worked out for laser spot input diameters less than 1.0 mm. For the Takata thermal skin model, Figure 3 shows the data of power and spot size in terms of the fluence or radiant exposure in Joules per square centimeter (Jcm^{-2}) necessary to produce the minimal observable 2^{nd} degree burn injury on the area of the exposure. For spot sizes greater than 1 mm in diameter there is very little dependence on the area and the

irradiance remains essentially constant, in contrast to actual ED_{50}'s below 1.0 mm the Takata values show a slight dependence on laser spot size as the diameter decreases.

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